1637

PATENT
Attorney Docket No. 02481.1743

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	)	
E. UHLMANN et al.	)	
	)	
Application No.: 09/835,371	)	Group Art Unit: 1637
	)	
Filed: April 17, 2001	)	Examiner: J. SIEW
	)	
For: POLYAMIDE NUCLEIC ACID DERIVATIVES AND AGENTS AND PROCESSES FOR PREPARING THEM	)	

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REQUEST FOR RECONSIDERATION

Sir:

This paper is being filed in response to the Office Action dated April 24, 2003. Applicants respectfully request reconsideration and withdrawal of the rejections set forth in the Office Action in view of the following remarks. Claims 1-81 are pending in this application, only claims 1-25, 31, 32, and 40-80 having been examined on the merits in the Office Action.

REMARKS

I. *Information Disclosure*

The Office indicates that the two Information Disclosure Statements filed by Applicants (and references cited in them) are not in the Office's file, and requests that Applicants re-submit both Statements, along with the cited references. (Office Action at paragraph 2.) Attached to this Request is a copy of the two Information Disclosure Statements, along with the accompanying Forms PTO-1449 and cited references. Also attached are copies of stamped

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postcards, indicating that the attached papers and references were received by the Office on October 26, 2001, and March 15, 2002. Because the attached papers and references were timely filed in complete form, Applicants believe that no petition or fee is due for re-submission of them. However, if any petition or fee is required, please grant the petition and charge the fee to our deposit account 06-0916.

II. *Restriction Requirement*

The Office makes the Restriction Requirement FINAL. (Office Action at paragraph 3.) Applicants respectfully submit that the claims of elected Group I are related to those of non-elected Group II as a product and a process of using. The claims of elected Group I are related to those of non-elected Group III as a product and a process of making. Applicants respectfully submit that, in accordance with MPEP § 821.04, the non-elected process claims of Groups II and III should be rejoined with the product claims of Group I once one or more product claims are found to be allowable.

III. *Rejections Under 35 U.S.C. § 102*

A. Uhlmann *et al.*

The Office rejects claims 3-20 and 45-80 under 35 U.S.C. § 102(b) as anticipated by Uhlmann *et al.* (*Nucleosides and Nucleotides*, 1997). (Office Action at paragraph 5.) The Office asserts that *Uhlmann* teaches polyamide nucleic acids with N-(2-aminoethyl)glycine units, and that this teaching anticipates present claims 3-20 and 45-80. The Office does not identify the specific compound in *Uhlmann* that supposedly anticipates the compounds of claims 3-20 and

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45-80. Applicants respectfully submit that *Uhlmann* does not disclose a compound according to present claims 3-20 and 45-80, and thus does not anticipate these claims.

Present claim 3, and thus its dependent claims 4-20 and 45-80, recite a PNA derivative that carries one or more phosphoryl radicals at the C-terminus or at the C- and N-termini of the PNA backbone. The structures disclosed by *Uhlmann* on pages 603 (the unmodified PNA), at the bottom of page 604, and on page 606, do not anticipate any of claims 3-20 and 45-80 because, among other reasons, they do not possess a phosphoryl radical at the C- or N-terminus.

With regard to the structure disclosed by *Uhlmann* at the top of page 604 (PHONA), Applicants submit that the PHONA of *Uhlmann* cannot be constructed from the formula recited in present claim 3. For example, D′ and {POLY} of the formula of present claim 3 do not include phosphoryl radicals. Furthermore, the definition of {POLY} in claim 3 does not encompass the phosphonate ester linkage present in the PHONA of *Uhlmann.* Accordingly, the PHONA disclosed by *Uhlmann* on page 604 does not anticipate claims 3-20 and 45-80.

With regard to the structures disclosed by *Uhlmann* on page 607 (and the PHONA disclosed at the top of page 604), Applicants submit that none of these structures can be constructed from the formula recited in present claim 3. More specifically, present claim 3, and thus its dependent claims 4-20 and 45-80, recite a PNA derivative of Formula I.

The Office asserts that, when q = 0, m = 0, n = 0, and {POLY} = Formula IIIB in Formula I, the PNA derivative of claim 3 is the same compound as a compound disclosed by *Uhlmann* (presumably meaning the structures recited on page 607). Applicants respectfully submit that it appears that the Office has misinterpreted the structure represented by Formula I in claim 3. More specifically, it appears that the Office has constructed a PNA derivative according

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to Formula I of claim 3 by using Formula IIIB as the {POLY} unit in Formula I. Applicants submit that this is not consistent with the formula of Formula I. That is, in Formula I, {POLY} is defined by Formula II, which comprises at least one {BLOCK} unit bonded to element "G". The {BLOCK} unit may be defined by Formula IIIB, but that does not eliminate the requirement for that unit to be bound to "G" in order to complete the structure of {POLY}. "G" is defined in claim 3 as $(CR_5R_6)_{u'}$, $C(O)NH\text{-}(CR_1R_2)_{t'}$, or $C(O)NH\text{-}(CH_2CH_2O)_u\text{-}CH_2CH_2$, wherein u' is from 1 to 10 and t' is from 2 to 10. The {POLY} unit is bonded to "V", which is oxygen, sulfur, or NR_1 (not CH_2, as would be required if the structures of *Uhlmann* were included within the formula of present claim 3). In other words, the structures disclosed by *Uhlmann* on page 607 (as well as the PHONA disclosed on page 604) are not encompassed by the formula recited in present claim 3 because these structures of *Uhlmann* do not include an oxygen, sulfur, or NR_1 group attached to a phosphorus atom at the C-terminus (*i.e.*, they do not satisfy element "V" of the structure recited in claim 3).

Applicants submit that *Uhlmann* does not disclose a PNA derivative according to present claim 3 when {POLY} is properly defined according to the terms of claim 3. Because claims 4-20 and 45-80 depend from claim 3, and thus include all of the elements of the PNA derivative recited in claim 3, *Uhlmann* likewise does not disclose a PNA derivative according to present claims 4-20 and 45-80. Therefore, Applicants respectfully request that the Office reconsider and withdraw the rejection of claims 3-20 and 45-80 as anticipated under 35 U.S.C. § 102(b) by *Uhlmann*.

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B. Breipohl *et al.*

The Office rejects claims 1-20, 23, 25, 30-32, and 40-80 under 35 U.S.C. § 102(b) as anticipated by Breipohl *et al.* (U.S. Patent No. 6,046,306). (Office Action at paragraph 6.) The Office asserts that *Breipohl* teaches labelled polyamide nucleic acids, and that this teaching anticipates present claims 1-20, 23, 25, 30-32, and 40-80. The Office does not identify the specific compound in *Breipohl* that supposedly anticipates the PNA derivative of claims 1-20, 23, 25, 30-32, and 40-80. Applicants respectfully submit that *Breipohl* does not disclose a PNA derivative according to present claims 1-20, 23, 25, 30-32, and 40-80.

Present independent claim 1 recites a PNA derivative which carries one or more phosphoryl radicals at the C terminus or at the C and N termini of the PNA backbone. Present independent claim 3 recites a PNA derivative of a given formula, which includes phosphoryl groups at both the N-terminus and C-terminus of the PNA backbone. Claims 2, 4-20, 23, 25, 30-32, and 40-80 all depend from either claim 1 or claim 3. Thus, if *Breipohl* does not anticipate claim 1 and claim 3, it does not anticipate claims 2, 4-20, 23, 25, 30-32, and 40-80.

Applicants submit that *Breipohl* does not disclose a PNA derivative which carries one or more phosphoryl radicals at the C-terminus or at the C-and N-termini of the PNA backbone. As mentioned above, the Office does not identify any such PNA derivative. In view of the lack of disclosure of such a PNA derivative, *Breipohl* does not anticipate either claim 1 or claim 3. Accordingly, *Breipohl* does not anticipate claims 2, 4-20, 23, 25, 30-32, and 40-80. Therefore, Applicants respectfully request that the Office reconsider and withdraw the rejection of claims 1-20, 23, 25, 30-32, and 40-80 as anticipated under 35 U.S.C. § 102(b) by *Breipohl*.

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IV. *Rejections Under 35 U.S.C. § 103*

A. Uhlmann *et al.* in view of Weiler *et al.*

The Office rejects claims 23 and 24 under 35 U.S.C. § 103(a) as unpatentable over Uhlmann *et al.* in view of Weiler *et al.* (Nucl. Acids Res. 1997). (Office Action at paragraph 7.) The Office relies on *Uhlmann* for the teaching of polyamide nucleic acids with N-(2-aminoethyl)glycine units, but asserts that *Uhlmann* does not disclose microarray supports for these PNAs. The Office asserts, however, that *Weiler* teaches the construction of PNA microarrays. The Office then concludes that it would have been obvious to construct microarrays using *Uhlmann's* PNAs. Applicants respectfully submit that, regardless of whether it would be obvious to use *Uhlmann's* PNAs in *Weiler's* microarrays, the combination of *Uhlmann* and *Weiler* does not render present claims 23 and 24, or any other claim of this application, obvious.

Initially, Applicants note that present claims 23 and 24 are not directed to microarrays. Accordingly, the rationale for the Office's rejection is inapplicable, and Applicants request that the Office withdraw the rejection. To expedite allowance of the present claims, Applicants will address the rejection as it applies to the subject matter claimed in claim 31, which is directed to the subject matter addressed in the Office Action.

Present claim 31 recites a PNA chip comprising a PNA derivative as claimed in claim 1 and a substrate suitable for fabricating a microarray. For the reasons discussed above, Applicants submit that *Uhlmann* does not disclose or suggest the PNA derivative of claim 1. Thus, to render claim 31 obvious, *Weiler* must at least disclose or suggest the PNA derivative of claim 1, in addition to teaching the use of such PNA derivatives in microarrays. Applicants submit that *Weiler* does not teach either of these.

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Weiler describes the synthesis of macroscopic arrays of unmodified PNAs on membranes, and various hybridization studies based on these arrays. However, *Weiler* does not disclose or suggest the PNA derivative of present claim 1.

Furthermore, *Weiler* is limited to macroarrays, whereas present claim 31 is directed to microarrays. The differences between the macroscopic array described by *Weiler* and the microarrays of claim 31 is more than just semantic in nature, due both to the inherently different chemistry and technology requirements for their synthesis, as well as the possibility of massively parallel hybridization experiments using microarrays (which are not possible using macroarrays).

Finally, *Weiler* does not disclose or suggest the synthesis, or advantages, of arrays of PNA derivatives carrying one or more phosphoryl radicals at their C-termini or at both their C- and N-termini.

For at least these reasons, Applicants submit that the combination of *Uhlmann* and *Weiler* fails to render present claim 31 obvious. Accordingly, Applicants submit that present claim 31 is patentable under 35 U.S.C. § 103(a) over the combination of *Uhlmann* and *Weiler*.

B. Breipohl *et al.* in view of Weiler *et al.*

The Office rejects claims 23 and 24 under 35 U.S.C. § 103(a) as unpatentable over Breipohl *et al.* in view of Weiler *et al.* (Office Action at paragraph 8.) The Office relies on *Breipohl* to teach labelled polyamide nucleic acids. The Office asserts that *Breipohl* does not teach microarrays, but that *Weiler* teaches construction of PNA microarrays. The Office then concludes that it would have been obvious to construct microarrays using *Breipohl's* PNAs. Applicants respectfully submit that, regardless of whether or not it would be obvious to use

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Breipohl's PNAs in *Weiler's* microarrays, the combination of *Breipohl* and *Weiler* does not render present claims 23 and 24, or any other claim of this application, obvious.

Initially, Applicants note that present claims 23 and 24 are not directed to microarrays. Accordingly, the rationale for the Office's rejection is inapplicable. Furthermore, the discussion presented under this rejection focuses on the asserted teachings of *Uhlmann* in view of *Weiler*, whereas the rejection is based on the combined teachings of *Breipohl* and *Weiler*. For at least these reasons, the rejection is improper, and should be withdrawn.

However, as with the previous rejection, to expedite allowance of the present claims, Applicants will address the rejection as it is set forth over the combined teachings of *Breipohl* and *Weiler* (not *Uhlmann* and *Weiler*), and as it applies to the subject matter claimed in claim 31, which is directed to the subject matter addressed in the Office Action.

As discussed above, present claim 31 recites a PNA chip comprising a PNA derivative as claimed in claim 1 and a substrate suitable for fabricating a microarray. For the reasons discussed above, Applicants submit that *Breipohl* does not disclose or suggest the PNA derivative of claim 1. Thus, to render claim 31 obvious, *Weiler* must at least disclose or suggest the PNA derivative of claim 1, in addition to teaching the use of such PNA derivatives in microarrays. Applicants submit that *Weiler* does not teach either of these.

Weiler describes the synthesis of a macroscopic arrays of unmodified PNAs on membranes, and various hybridization studies based on these arrays. However, *Weiler* does not disclose or suggest the PNA derivative of present claim 1.

Furthermore, *Weiler* is limited to macroarrays, whereas present claim 31 is directed to microarrays. The differences between the macroscopic array described by *Weiler* and the

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microarrays of claim 31 is more than just semantic in nature, due both to the inherently different chemistry and technology requirements for their synthesis, as well as the possibility of massively parallel hybridization experiments using microarrays (which are not possible using macroarrays).

Finally, *Weiler* does not disclose or suggest the synthesis, or advantages, of arrays of PNA derivatives carrying one or more phosphoryl radicals at their C-termini or at both their C- and N-termini.

For at least these reasons, Applicants submit that the combination of *Breipohl* and *Weiler* fails to render present claim 31 obvious. Accordingly, Applicants submit that present claim 31 is patentable under 35 U.S.C. § 103(a) over the combination of *Breipohl* and *Weiler*.

C. Uhlmann *et al.* in view of Manoharan *et al.*

The Office rejects claims 21 and 22 under 35 U.S.C. § 103(a) as unpatentable over Uhlmann *et al.* in view of Manoharan *et al.* (U.S. Patent No. 6,043,352). (Office Action at paragraph 9.) The Office relies on *Uhlmann* for the teaching of polyamide nucleic acids with N-(2-aminoethyl)glycine units. The Office asserts that *Uhlmann* does not disclose a pharmaceutical composition comprising a PNA, or targeting of a PNA to the HA ras translation start site, but that *Manoharan* teaches use of PNAs, and in particular PNAs specific for the HA ras translation start site, in pharmaceutical compositions. The Office then concludes that it would have been obvious to make a pharmaceutical composition comprising a PNA according to *Uhlmann* that is specific for the HA ras translation start site, as taught by *Manoharan*. Applicants respectfully submit that, regardless of whether or not it would be obvious to use *Uhlmann's* PNAs in *Manoharan's* pharmaceutical compositions, the combination of *Uhlmann* and *Manoharan* does not render present claims 21 and 22 obvious.

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Claims 21 and 22 depend from claim 3. For the reasons discussed above, Applicants submit that *Uhlmann* does not disclose or suggest a PNA derivative according to claim 3. In order for the combination of *Uhlmann* and *Manoharan* to render claims 21 and 22 obvious, *Manoharan* must disclose or suggest at least a PNA derivative according to Formula I in which the {POLY} unit comprises Formula IIIB bound to "G", a compound having an element "V" according to the formula recited in claim 3, or modifying the PNA of *Uhlmann* to include a {POLY} unit comprising Formula IIIB bound to "G" or a compound having an element "V" according to the formula recited in claim 3. Applicants submit that *Manoharan* does not disclose or suggest such a PNA derivative or such a modification to *Uhlmann's* PNA. The Office has not identified any such teaching, and Applicants have found no such teachings in *Manoharan.*

Because the combination of *Uhlmann* and *Manoharan* fails to disclose or suggest the PNA derivatives of present claim 3, the combination fails to render the PNA derivatives of present claim 3 obvious. Accordingly, the combination of *Uhlmann* and *Manoharan* cannot render the PNA derivatives of claims 21 and 22 obvious. For at least this reason, Applicants submit that claims 21 and 22 are patentable under 35 U.S.C. § 103(a) over the combination of *Uhlmann* and *Manoharan.* Therefore, Applicants respectfully request that the Office reconsider and withdraw the rejection of claims 21 and 22 under 35 U.S.C. § 103(a) as unpatentable over *Uhlmann* in view of *Manoharan.*

V. *Conclusion*

Applicants submit that present claims 1-25, 31, 32, and 40-80 are neither anticipated nor rendered obvious by the cited references. Therefore, Applicants request that the Office withdraw

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the rejections set forth in the Office Action, rejoin method claims 26-29, 33-39, and 81, and permit this application to issue as a U.S. patent in due course. If the Office believes anything further is necessary in order to place this application in even better condition for allowance, Applicants request that their undersigned representative be contacted at the telephone number or e-mail address below to discuss the remaining issues.

Please grant any extension of time required to enter this response and charge any required fee to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
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By: _____
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Date: July 24, 2003

Attachments:
Re-submission of IDS/PTO-1449/references
of October 26, 2001 and March 15, 2002

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